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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/801,185	03/07/2001	Jochen G. Salfeld	BBI-043CPUSCN	1672

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EXAMINER	
SAUNDERS, DAVID A	

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 06/13/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
801,185	SALFELD et al.
Examiner	**Group Art Unit**
SAUNDERS	1647

—The MAILING DATE of this communication appears on the cover sheet beneath the correspondence address—

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, such period shall, by default, expire SIX (6) MONTHS from the mailing date of this communication .
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).

Status

☑ Responsive to communication(s) filed on 2/24/05.

☑ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle,* 1935 C.D. 1 1; 453 O.G. 213.

Disposition of Claims

☑ Claim(s) 74-89, 91, 93, 95, 97, 99-104, 106, 108, 110, 112, 114-127, 129-133, 135, 137-142 is/are pending in the application.

Of the above claim(s) _____ is/are withdrawn from consideration.

☑ Claim(s) 115-121, 141-142 is/are allowed.

☑ Claim(s) 74-89, 91, 93, 95, 97, 99-104, 106, 108, 110, 112, 114, 122-127, 129-133, 135, 138-140 is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claim(s) _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119 (a)-(d)

☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 11 9(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 1 7.2(a)).

*Certified copies not received: _____.

Attachment(s)

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Reference(s) Cited, PTO-892

☐ Notice of Informal Patent Application, PTO-152

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Other _____

Office Action Summary

The amendment of 2/24/05 has been entered. Claims 74-89, 91, 93, 95, 97, 99-104, 106, 108, 110, 112, 114-127, 129-133, 135 and 137-142 are pending and under examination.

The amendment has overcome the following objections/rejections stated in the office action of 8/24/04:

1) The objections to claims 88, 101, 103, 120 and 139.

2) The 112 second para. rejections of claims 88, 91-98, 103, 106-113 and 122..

3) The 112, first paragraph rejection of claims 83, 90, 105, 122, 124 and 130 set forth at page 7.

The following new grounds of objection are stated:

Claims 125, 127, 129, 131-133 are objected to because of the following informalities: Each of claims 125, 129 and 131-133 ends with two periods. In claim 127, a comma is missing after "IL-6" (line 12). Appropriate correction is required.

Applicant's amendment has necessitated the following new grounds or a modification of previously stated grounds of rejection under 112:

Claims 84-89, 91, 93, 95, 97, 99-104, 106, 108, 110, 114, 123-127, 129-133 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the

claimed invention. Claims 84-87 and 99-102 contain new matter; in the Markush group instead into each. All dependent claims are listed in the rejection.

Applicant considers that the amendment of these claims is supported by page 29, line 28-page 31, line 12. The examiner notes, first, that this passage was specifically directed to the treatment of rheumatoid arthritis (RA), rather than for treatment of a "disorder in which TNF alpha activity is detrimental". From applicant's urgings it is apparent that he considers any one of the particular conditions noted at pages 29-40 as being examples of such "disorders". The examiner however considers that the listing of secondary agents for the treatment of arthritis set forth at pages 29-31 was carefully selected from what was art known to be those agents that are suitable for treatment of RA; likewise the secondary agents listed for any of the other disorders set forth at pages 31-40 were carefully selected for each particular disorder. For example gold is listed as a secondary agent for treating RA (page 31, line 1) but no other disorder.

Also it is noted that the Markush group of secondary agents recited in claim 86 etc. includes numerous subgenuses which would not be applicable for the treatment of transplant rejection as a disorder. Of the secondary agents listed at page 38 for the treatment of this disorder, only the subgenus of claim 88 recited, as "a secondary antibody" would at all encompass anything listed.

It is therefore considered that applicant's original disclosure was directed to combinations of the instant anti – TNF alpha antibody and a secondary agent, wherein the secondary agents were contemplated as being useful for the treatment of one or

more particular disorders, but not for the treatment of the genus of disorders. Applicant cannot now play a game of mixing and matching with respect to the secondary agents used in the treatment of disorders.

Second, even if the above basis of rejecting the claims on new matter were in error, the examiner considers that certain Markush group members introduced into claims 84-87 and 99-102 themselves introduce new matter.

Applicant recites the new subgenus listed as "a secondary antibody". Numerous specific examples of these are listed for the treatment of RA at pages 29-31. Numerous specific examples of such are listed for the treatment of transplant rejection at page 38; some antibodies are used in the treatment of either disorder; some are used in the treatment of only one of the two disorders. In any event, the specific antibodies listed are directed against a diverse group of antigens, some of which are secreted and some of which are all surface bound (in that case not even limited to one type of cell). Thus no particular antibody listed is representative of the subgenus; applicant was thus not in possession of the subgenus of "secondary" antibodies.

In like manner, applicant recites the new subgenus listed as "a fusion protein" in claims 84-87 and 99-102. Applicant has "recited fusion protein" at pages 29-40 for treatments of RA, IBD, MS, sepsis and ARDS. In each case, only two particular fusion proteins are listed: both have a TNF receptor fused to IgG. These two examples utterly fail to support a secondary therapeutic agent that is any protein fused to any other protein.

With respect to dependent claims 88 and 103, it is noted that all but two of the listed antibodies are derived from the disclosure at pages 29-31 concerning RA. Of the two not listed for RA, "anti-IL-6" is disclosed for treatment of IBD (page 31, lines 18-19, in which case the antibody is "monoclonal" rather than merely "antibody") and no other disorder, and "anti IL-8" is disclosed for treatment of ARDS (page 32, line 30) and no other disorder. Thus, again, the examiner considers that each species of secondary agent listed in the specification was listed after a careful consideration of what secondary agents are particularly suitable for any given disorder. Applicant cannot therefore mix and match embodiments in a random manner.

Claim 122 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claim 122 recites new matter.

Claim 122 is recited with a Markush group of additional agents; these agents were listed as pertaining to the treatment of certain diseases listed at spec.pages 29-32. None of the diseases contemplated at pages 29-32 included "periodontal disease, obesity, and radiation toxicity", which are the diseases recited in base claim 118 and which would be treated in the method of dependent claim 122. Applicant has thus improperly extended the originally disclosed treatment method of a new group of diseases.

As stated further supra regarding claims 84-88 and 99-103, there is no basis for applicant to mix and match the secondary agents disclosed for particular diseases/disorders with any of the other diseases/disorders recited in the original disclosure.

Claims 123 and 129 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. These claims recite new matter because of the insertion of the Markush group member "T-614".

Page 30, line 18 lists T-614 as a "cytokine inhibitor" rather than as a "cytokine suppressive anti-inflammatory drug" (CSAID). Applicant is thus applying a new description of the properties of T-614 by inserting it on a claim listing members of a Markush group of CSAIDS.

The examiner further notes that claims 123 and 129 are of undue scope by not being limited to treatment of RA. These two agents are only listed in the paragraph spanning pages 29-30-31, which lists agents for the treatment of RA, not of a generic "disorder".

Claims 124 and 130 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed,

had possession of the claimed invention. These claims recite new matter because of the insertion of the Markush group member "leflunomide".

Page 30, lines 14-15 lists leflunomide as an "anti-inflammatory and cytokine inhibitor" rather than as a "NSAID". It therefore appears that recitation of "leflunomide" may be proper in claims 123 and 129, but not in claims 124 and 130.

Again the examiner notes that this "leflunomide" member was only disclosed for treatment of RA, and not of a generic disorder. Numerous other members if claims 124 and 130 were only disclosed for the treatment of particular disorders and not for treatment of generic disorders.

Claims 125 and 131 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claims 125 and 131 are of undue scope by not being limited to the treatment of RA. The four listed cytokines only appear together in the paragraph spanning pages 29-30-31, which lists agents for the treatment of RA, not of a generic disorder.

The examiner further notes that a completely different group of cytokines is listed (page 32, lines 10-11) for the treatment of sepsis. The examiner notes that no cytokine is listed for the treatment of transplant rejection (page 38). It is therefore taken that each listing of secondary agents set forth in the specification was intended to only apply to the treatment of each particularly recited condition; applicant cannot now mix and

match secondary agents and particular disorders in a willy nilly manner without entering new matter.

Claims 126 and 132 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claims 126 and 132 are of undue scope by not being limited to treatment of RA. The four listed fusion, proteins were listed together in the para. spanning pages 29-30-31 for the treatment of RA; no other disorder disclosed at pages 31-32 has a listing of the members DAB-IL-2 and DAB 389 –IL-2;

again, the examiner considers that each listing of secondary agents for the treatment of a given disorder was only intended to apply to that disorder.

Claims 127 and 133 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claims 127 and 133 contain new matter as noted previously and due to the added Markush group members in the amendment of 2/24/05.

Claims 127 and 133 recite a mongrel Markush group of secondary agents. Those listed through "clabribine" (line 11) and those listed as "prednisolone, methylprednisolone" (line 19) have been disclosed at page 31, lines 33-page 32, line 1

for the treatment of MS. Those listed through "anti Endotoxin peptides" (line 16) are disclosed at page 32, lines 7-27 for the treatment of sepsis. The "surfactant replacement therapy (lines 16-17) is disclosed at page 32, line 30 for the treatment of ARDS. The agents listed as "IL-4 agonists" (line 17) through "prednisone" (line 19) and as "gold" (line 19) through "azaribrine" (line 27) have been disclosed at page 29, line 30-page 31, line 12 for the treatment of RA. Those listed as "budenoside" (line 27) through "bignocaine" (line 33) have been disclosed at page 31, lines 15-30 for the treatment of MS. Because the claims are not recited such that only the particularly taught diseases are each treated with only the therapeutic agents particularly disclosed therefore, applicant has improperly extended the scope of the originally disclosed treatment methods.

Claims 135 and 138-140 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Each of these claims has inserted a Markush group of agents for the treatment of RA. Among these members "prednisolone" and "methylprednisolone" have been originally disclosed (page 31, line 33) for the treatment of MS, rather than RA. Applicant is therefore claiming use of a drug combination that was not originally contemplated.

By way of summary regarding the new matter rejections of record and/or modified because of applicant's amendment, the examiner does not consider the listing

of secondary agents for any one disease to be applicable for another disease/disorder. The examiner has noted examples in which an agent (e.g. gold) has been listed for the treatment of one disorder and no other. The examiner also notes that there are cases in which what is listed as a secondary agent for one disorder is contradicated for another disorder. For example, at page 31, line 18 applicant lists "anti-IL-6" as a secondary agent for the treatment of RA, while at page 36, line 23 applicant lists "the cytokine interlinkin –6" as a secondary agent for the treatment of sepsis, applicant cannot thus first arbitrarily lift out an agent recited at some location in the disclosure for the treatment of a particular disease and recite that agent as being suitable for the treatment of another disease/disorder.

To further elaborate, the examiner notes that whole subgenuses of secondary agents that applicant has lifted out of the description of agents used to treat RA (in some cases creating new matter in so doing) are missing from the lists of agents recited for other diseases. For example the treatment of sepsis set forth at page 36 discloses no use of a NSAID or CSAID; also the examiner finds no mention of any NSAID or CSAID in the treatments of transplant rejection and malignancy (page 38).

Likewise the examiner finds "cyclosporin A or FK506" mentioned as a secondary reagent for the treatment of transplant rejection (page 38), and not for any other disorder.

Given that one of skill would recognize disorders such as rheumatoid arthritis, ARDS, sepsis, transplant rejection and malignancy as diverse diseases that have differing mechanisms by which they incur disorder; the examiner cannot concur that one

of skill would have recognized any agent listed for one disease/disorder would be used for the treatment of another disorder.

Finally, applicant has urged (page 230 that literal support for claim amendments is not required, and has cited Fujikawa v. Wattanasin 39 USPQ2d 1895. This case is not on point, since therein the CAFC did affirm the BPAI's refusal to enter a new claim that lacked ipsis verbis support and since a large number of compounds were disclosed and nothing in the teachings pointed out the new subgenus.

Instantly the examiner finds that a large number of compounds is described, but the subgenus of those compounds disclosed for each particular disorder was disclosed as such; and nothing in the disclosure particularly points the reader to any of the new subgenuses of compounds that applicant has carved out of the disclosure (e.g. rejection of claims 84-87 and 99-102 supra) or the expanded genus of disorders to which various recited subgenuses of compounds are applicable.

In view of the large number of claims and the large number of permutations and combinations of secondary agents and diseases that could be arbitrarily carved out of the specification, without any particular direction pointing out these permutations and combinations, it is proper for the office to require epsis verbis support.

Applicant has urged (page 25) that one of skill would have recognized that the additional/secondary agents listed at pages 29-32 for RA and MS could be used in combination with the anti-TNF-alpha antibody for any of the other disorders. This argument is basically one of obviousness. This is not the standard for determining

what is supported under 112, first paragraph. Lockwood v. American airlines 41 USPQ2d 1961.

Furthermore this argument is not supportable factually; as noted further supra "gold" (page 31, line 1) for treatment of RA and is not listed for any other disease; those of skill are not aware of other autoimmune diseases for which this agent may be efficacious. Orally administered "collagen" is listed at page 31, line 2 for treatment of RA and is not listed for any other disease; the autoimmune attack against collagen is unique to RA, and no one of skill would have recognized that this agent should administered to treat any and all other autoimmune diseases. The examiner could offer more examples wherein the agent is unique to treatment of a particular disease; this is deemed unnecessary, since one exception shoots down the thesis; applicant is thus required to claim the invention for the treatment of particular diseases with the secondary agents that were particularly disclosed as pertaining to each disease, rather than claiming the invention as he may have later realized that he could have claimed it at the time of filing.

Applicant's urgings concerning new matter filed on 2/24/05 have been considered but are unconvincing.

The obviousness type double patenting rejections are maintained.

Claims 74-82 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-8, 24-25 and 28 of U.S. Patent No. 6,090,382. Although the conflicting claims are not identical, they are not patentably distinct from each other because see reasons in action of 5/29/03.

Claims 74 and 83 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1 and 24-25 of U.S. Patent No. 6,090,382, in view of Aggarwal et al. See reasons in action of 5/29/03.

Claims 84-87, 89, 91, 93, 95, 97, 99-102, 104, 106, 108, 110, 112, 135 and 138-140 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 4-7, 15, 17, 22, 36-39, 69, 87 and 93 of U.S. Patent No. 6,509,015. Although the conflicting claims are not identical, they are not patentably distinct from each other because of reasons in the action of 5/29/03.

It is noted that applicant will file a disclaimer when claims are otherwise allowable.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David A. Saunders, PhD whose telephone number is 571-272-0849. The examiner can normally be reached on Monday-Thursday 8:00a.m to 5:30 pm. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on 571-272-0841. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

David A Saunders

Saunders/tgd
June 8, 2005

DAVID SAUNDERS
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ART UNIT ~~182~~ 1644